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A phase I dose-finding and pharmacokinetics study of CPC634 (nanoparticle entrapped docetaxel) in patients with advanced solid tumors.

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Background: CPC634 is a novel product with docetaxel temporarily entrapped within stabilized CriPecR nanoparticles. We performed the first-in-human study with CPC634 (NCT02442531).

Methods: Patients (≥ 18 years) received CPC634 intravenously either 3-weekly (Q3W) (part 1, 15-100 mg/m²), 2-weekly (Q2W) (part 2, 45 mg/m²) or Q3W with dexamethasone premedication (part 3) following a 3+3 design. Primary objectives were to assess safety, establish the maximum tolerated dose (MTD), recommended phase 2 dose (RP2D), and to evaluate the pharmacokinetic (PK) profile of CPC634. Results: Thirty-three patients (part 1; n = 24, part 2; n = 3, part 3; n = 6) were treated. Skin toxicity was dose limiting at doses > 60 mg/m² in part 1, and at a 45 mg/m² dose in part 2. Skin toxicity was cumulative but resolved after ceasing treatment. The MTD in part 1 was set at 70 mg/m². In part 3, the 60 mg/m² was explored which resulted in improved skin tolerability even after repeated administrations without dose limiting toxicities. The RP2D was therefore set at 60 mg/m² with dexamethasone premedication. Grade ≥ 3 adverse events (CTCAE version 4.03) were skin toxicity (21%), fatigue (8%), neutropenia (6%), peripheral sensory (8%) and motor neuropathy (4%), stomatitis (4%), infections (4%) and hypomagnesemia (3%). Alopecia grade 1 was reported in 15% of patients. CPC634 exhibited a dose-proportional PK profile. One partial response and sixteen cases of stable disease (RECIST 1.1) were confirmed in part 1 and in part 3 as best response. Conclusions: CPC634 could be administered safely but showed cumulative, though reversible skin toxicity at high doses. The RP2D was set at 60 mg/m² Q3W with dexamethasone premedication. Additional studies assessing the intratumoral exposure to CPC634 (NCT0371243) and a phase II efficacy study of CPC634 in patients with platinum resistant ovarian cancer (NCT03742713) is currently ongoing.